DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 28, 2009 has been entered.

2. Applicants' arguments, filed October 28, 2009, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1, 2, 4 - 6 and 13 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16 and 19 - 21 of copending Application No. 10/468742. This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed October 15, 2008 and April 28, 2009 and those set forth below.

Applicants request that this provisional rejection be held in abeyance.

Therefore, this rejection is MAINTAINED for the reasons of record previously set forth in the above referenced Office Actions.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 2, 4, 6 - 9, 13, 14, 18 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. (WO 02/067998) in view of Nsereko et al. (Biomaterials 2002). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed October 15, 2008 and April 28, 2009 and those set forth below.

Applicants traverse this rejection on the grounds that the average person in the art simply would not arrive at the Examiner's proposed construction without knowledge of the present invention. Nsereko describes the localized delivery of paclitaxel in solid tumors from chitin microparticles. Applicants do not accept the assertion that it would have been obvious to apply this teaching to the silicon containing anti-cancer compositions of Canham et al. as Nsereko et al. is concerned with an entirely different delivery system and the average skilled person would not consider the chitin microparticles of Nsereko et al. to be functionally equivalent. While chitin and silicon may both be biodegradable, there is nothing to suggest that they would degrade at the same rate which would result in different release rates of the drug. It would not be possible to predict the dose for silicon microparticles from the chitin studies of Nsereko. The Applicants disagree with the Examiner's interpretation that a higher dose can be administered with localized delivery but rather that the skilled person would interpret this as affording the possibility of reducing the dose while achieving an effective

concentration at the tumor. The ability to deliver such high doses without significant mortality represents a completely unexpected and significant advantage for the silicon microparticle formulations of the present invention.

These arguments are unpersuasive. Both Nsereko et al. and Canham et al. are concerned with the delivery of cytotoxic agents from biodegradable materials. Thus, the subject of these two pieces of art are analogous are functionally equivalent in that both a biodegradable particles that degrade over time to release agents that kill cancer cells. The fact that these materials degrade at different rates would provide motivation for one of ordinary skill in the art to prepare a drug delivery system with different release rates. Applicants present no other arguments and/or evidence to support their assertion that the average skilled person would not consider the chitin microparticles of Nsereko et al. to be functionally equivalent to the silicon particle of Nsereko et al., both of which are biodegradable, controlled release drug delivery systems.

The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results based on the particular cytotoxic drugs being used, the delivery system and the degradation rate of the delivery system. Note, in order to overcome a prima facie case of obviousness, it is incumbent upon the Applicant to provide comparative test evidence that demonstrates unexpected

superiority of the claimed compositions versus the closest prior art compositions, and not simply an advantage predictable from the prior art. See *In re Chapman*, 148 USPQ 711, 715 (CCPA, 1966). Moreover, such proffered comparisons must be commensurate in scope with the breadth of the claims. See *In re Clemens*, 206 USPQ 289, 296 (CCPA, 1980) and *In re Coleman*, 205 USPQ 1172, 1175 (CCPA 1980).

For the treatment of cancer, the goal of treatment with cytotoxic agents is to kill cancer cells and higher concentrations are more likely to kill cells. However, such high concentrations cannot be administered systemically without significant side effects to the healthy cells of the patient being treated. One way to reduce global side effects and to increase the killing of the cancerous cells is to deliver a high concentration to the local environment of the tumor. The particles of Canham et al. could thus be used to deliver a dose higher than the lethal dose for systemic administration as that concentration is only present in the microenvironment of the tumor. This could result in a lower overall dose being administered as compared to a higher overall dose of the drug when administered systemically to achieve a much lower, global concentration of the anti-cancer agent. Applicants have not presented any persuasive arguments or evidence as to why a person of ordinary skill in the art would arrive at a different conclusion.

In order to overcome a prima facie case of obviousness, it is incumbent upon the Applicant to provide comparative test evidence that demonstrates unexpected superiority of the claimed compositions versus the closest prior art compositions, and not simply an advantage predictable from the prior art. See *In re Chapman*, 148 USPQ

711, 715 (CCPA, 1966). Moreover, such proffered comparisons must be commensurate in scope with the breadth of the claims. See *In re Clemens*, 206 USPQ 289, 296 (CCPA, 1980) and *In re Coleman*, 205 USPQ 1172, 1175 (CCPA 1980). The data presented in the specification is not commensurate in scope with the claims and is not persuasive. Only claims 7 and 13 contain any limitations on the amount of active ingredient present in the pharmaceutical composition. Applicants have not presented sufficient evidence to establish unexpected results for the full scope pf the claim, e.g. the breadth of cytotoxic drugs and types of silicon which are claimed. It is also noted that none of the claims contain any limitations on the dose of the silicon microparticles that are administered in the method.

9. Claims 1, 2, 4 - 9, 13, 14, 18 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. and Nsereko et al. further in view of Canham et al. (US 6,322,895). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed October 15, 2008 and April 28, 2009 and those set forth herein.

Applicant has not specifically addressed this rejection other than referring to Canham – US 6,322,895, so the rejection is maintained for the reasons set forth above with regard to Canham WO'998 and Nsereko et al. set forth above.

10. Claims 1, 2, 4, 6 – 9, 13, 14, 18 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Canham (WO 02/067998) in view of Straub et al. (US

6,610,317). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed October 15, 2008 and April 28, 2009 and those set forth below.

Applicant traverses this rejection on the grounds that the porous matrix of Straub would not be considered by the average person in any way functionally equivalent to the silicon microparticles loaded formulations and so there would simply be no motivation to arrive at the present invention. The average skilled man would not consider the direct tumoral administration of the compositions of Straub relevant to the use of cytotoxic agent loaded porous silicon particles and would not be able to draw any conclusions as to the dose of silicon microparticles which would be safely and effectively delivered.

These arguments are unpersuasive. Both Canham WO'998 and Straub related to porous pharmaceutical formulations that are used to delivery cytotoxic agents although the basis of the porous material is different between the two. Applicant have not presented any persuasive arguments and/or evidence that these art not functionally equivalent. Applicants have also not presented any persuasive arguments as to why, as Canham WO'998 teaches that the particles can be delivered to the vascular system of the hepatic artery (p 5, ln 19 – 22) would not consider that these same particles could be directly administered to the tumor, as the porous particles containing cytotoxic agent in Straub are administered (col 2, ln 34 - 41).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the dose of silicon microparticles) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification

are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

11. Claims 1, 2, 4 – 9, 13, 14, 18, 19 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Canham WO'998 and Straub further in view of Canham US 6,322,895). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed October 15, 2008 and April 28, 2009 and those set forth herein.

Applicant has not specifically addressed this rejection other than referring to Canham – US 6,322,895, so the rejection is maintained for the reasons set forth above with regard to Canham WO'998 and Straub et al. set forth above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

NMW